REMARKS

Claims 9, 10, 13-15, 24-36 and 38-49 are pending in the present application. Claims 10, 13, and 14 are withdrawn. Claims 9, 15, 24-36 and 38-49 are rejected. By virtue of this response, claims 25, 26, 32, and 33 have been cancelled. Claims 9 and 30 have been amended. Upon entry of this amendment, claims 9, 15, 24, 27-31, 34-36, and 38-49 are under consideration.

Support for the amendment of claims 9 and 30 can be found, *inter alia*, at page 16, lines 7-11, and page 16, line 23 to page 17, line 3 of the specification, as well as previously pending claims 25 and 32.

With respect to claim amendments and cancellation, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Claims Rejections – 35 USC § 103

Rejections based on Zubiaga and Banholzer

Claims 9, 15, 24-27, 29-34, 36, 38-41 and 49 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Zubiaga et al. ("Zubiaga"), in view of Banholzer et al. ("Banholzer"). Applicants respectfully traverse this rejection.

Solely in an effort to expedite prosecution and without acquiescing to the rejection, independent claims 9 and 30 have been amended to recite "wherein said heterologous instability sequence DNA is from about 200 to about 1500 nucleotides in length and comprises DNA

corresponding to sequences that flank said mRNA instability sequence in the naturally occurring gene."

Zubiaga and Banholzer, alone or in combination, do not render the amended claims obvious. Specifically, Zubiaga focuses on the identification of the minimal AU-rich motif capable of destabilizing mRNA, and teaches that a nonamer sequence is effective in destabilizing mRNA independent of the sequence context in which it is present. See page 2225, left column of Zubiaga. Zubiaga is completely silent about using longer sequences (namely, sequences of 200 to about 1500 nucleotides in length) and including sequences that flank the mRNA instability sequence in the naturally occurring gene. On the contrary, for the purpose of defining the minimal AU rich motifs capable of destabilizing mRNA, one of ordinary skill in the art would not choose to use flanking sequences which may interfere with the determination.

Banholzer focuses on understanding the mechanisms by which rapamycin downregulates IL-3 mRNA in a tumor mast cell line. To determine whether the 3'UTR of IL-3 confers sensitivity to a heterologous transcript, Banholzer examined the effect of rapamycin on AP receptor constructs carrying the 3'UTR of IL-3. They concluded that "IL-3 3'UTR could confer RAPA sensitivity to reporter transcripts, provided that the 3'UTR sequence was intact." Banholzer thus conveys to a person of ordinary skill in the art that, for the purpose of studying the effect of rapamycin on IL-3 3'UTR, it is important to keep the mRNA instability sequence in its natural state.

Given the teaching of Zubiaga and Banholzer, a person of ordinary skill in the art would not choose to use the heterologous expression construct of Zubiaga, designed to identify the minimal AU rich sequence motif that destabilizes mRNA independent of the sequence context in which is present, to screen or assay for compounds that affect the stability of specific mRNAs. This is particularly true because Banholzer teaches that, for the purpose of studying the effect of a compound on a specific mRNA, it is desirable to keep the mRNA instability sequence in its natural state, rather than inserting it artificially into a 3'UTR that is heterologous to the mRNA instability sequence.

Accordingly, Applicants respectfully request that the 35 U.S.C. § 103(a) rejection based on Zubiaga and Banholzer be withdrawn.

Rejections based on Zubiaga, Banholzer, and Lemm and Ross

Claims 28 and 35 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Zubiaga et al. ("Zubiaga") in view of Banholzer et al. ("Banholzer"), as applied to claims 9, 15, 24-27, 29-34, 36, 38, 39, 41 and 49, and further in view of Lemm and Ross (Molecular and Cellular Biology, 2002, Vol. 22, No. 12, pages 3959-3969). Applicants respectfully traverse this rejection.

As discussed above, Zubiaga or Banholzer, alone or in combination, do not render claims of the present application obvious.

Lemm and Ross is cited as disclosing that a 249 nucleotide coding region from c-myc destabilizes c-myc and that such sequence destabilizes beta-globin mRNA when inserted in frame within the coding region of beta-globin. Applicants respectfully submit that Lemm and Ross not only does not cure the deficiencies of Zubiaga and Banholzer discussed above, but also teaches away from claims 28 and 35 of the present application.

As discussed in Lemm and Ross, the coding region instability determinant (CRD) functions independently of the AU-rich element to make the mRNA instable. Lemm and Ross teaches that the CRD "must be translated to destabilize the mRNA," and that "[p]lacing a translational stop codon upstream of the CRD stabilizes the chimeric RNA." Page 3959. Lemm and Ross further discusses regulation of c-myc mRNA decay by "translational pausing" in the CRD. One of ordinary skill in the art reading Lemm and Ross will clearly understand that the CRD has to be present in the coding region in order for "translational pausing" to occur, and that placing the CRD into the 3'UTR would be ineffective in destabilizing mRNA.

Accordingly, Applicants respectfully submit that Lemm and Ross teaches away from inserting an CRD into an heterologous 3'UTR construct of Zubiaga, which is designed to identify the minimal AU rich sequence motif that destabilizes mRNA. Applicants respectfully request withdrawal of the 35 U.S.C. § 103 rejection.

Rejections based on Zubiaga, Banholzer, in combination with other references disclosing specific mRNA instability sequences

Claims 43 and 47 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Zubiaga in view of Banholzer, as applied to claims 9, 15, 24-27, 29-34, 36, 38, 39, 41 and 49, and further in view of Kastelic et al. ("Kastelic," Cytokine, 1996, Vol. 8, No. 10, pages 751-761). Claim 48 is rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Zubiaga in view of Banholzer, as applied to claims 9, 15, 24-27, 29-34, 36, 38, 39, 41 and 49, and further in view of Levy et al. ("Levy," JBC, 1996, Vol. 271, No. 5, pages 2746-2753). Claim 44 is rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Zubiaga in view of Banholzer, as applied to claims 9, 15, 24-27, 29-34, 36, 38, 39, 41 and 49, and further in view of Rajagopalan et al. ("Rajagopalan," Journal of Neurochem. 2000, Vol. 74, pages 52-59). Claim 45 is rejected under 35 U.S.C. § 103(a) as being patentable over Zubiaga in view of Banholzer, as applied to claims 9, 15, 24-27, 29-34, 36, 38, 39, 41, and 49, and further in view of Capaccioli et al. ("Capaccioli," Oncogene, 1996, Vol. 13, pages 106-115). Claim 46 is rejected under § 103(a) as allegedly being unpatentable over Zubiaga in view of Banholzer, as applied to claims 9, 15, 24-27, 29-34, 36, 38, 39, 41 and 49, and further in view of Yeilding et al. ("Yeilding," Molecular and Cellular Biology, 1996, Vol. 16, No. 7, pages 3511-3522). Applicants respectfully traverse these rejections.

As discussed above, Zubiaga or Banholzer, alone or in combination, do not render claims of the present application obvious.

None of the other cited references cures the deficiencies discussed above. Specifically, Kastelic, Levy, Rajagopalan, Capaccioli, Yeilding are each cited as disclosing a specific mRNA

instability sequence. These references do not teach or suggest stable cell lines or set of stable cell lines claimed in the present application.

Accordingly, Applicants respectfully request withdrawal of the 35 U.S.C. § 103 rejections.

Rejection based on Zubiaga, Banholzer, and Zhang

Claim 42 is rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Zubiaga in view of Banholzer, as applied to claims 9, 15, 24-27, 29-34, 36, 38, 39, 41 and 49, and further in view of Zhang et al. ("Zhang," Biochemical and Biophysical Research Communications, 1996, Vol. 227, No. 3, pages 707-711). Applicants respectfully traverse this rejection.

As discussed above, Zubiaga or Banholzer, alone or in combination, do not render claims of the present application obvious.

Zhang does not cure the deficiencies discussed above. Specifically, Zhang is cited as disclosing reporter genes, such as GFP. Zhang does not teach or suggest stable cell lines or set of stable cell lines claimed in the present application.

Accordingly, Applicants respectfully request withdrawal of the 35 U.S.C. § 103 rejection.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 608352000100. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: February 17, 2009

Respectfully submitted,

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